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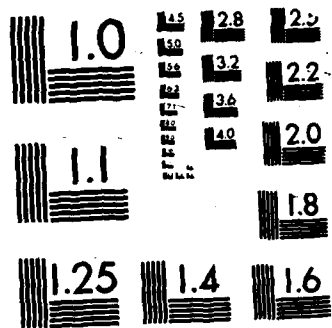
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INFLUENCE OF ATROPINE ON PHYSICAL PERFORMANCE IN THE HEAT

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OF
ENVIRONMENTAL MEDICINE
Natick, Massachusetts

MAY 1986

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DISCLAIMERS

Human subjects participated in these studies after giving their free and informed voluntary consent. Investigators adhered to AR 70-25 and USAMRDC Regulation 70-25 on Use of Volunteers in Research.

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FOREWORD

This study was conducted at USARIEM as part of an interdivisional effort to identify the physiological and medical limitations of atropine on soldier performance. This report focuses on muscular strength, muscular endurance and gross motor performance. Other aspects of the study are covered under two previously published reports (14,19).

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ABSTRACT

Atropine is the antidote of choice used in the treatment of exposure to cholinesterase inhibiting substances. To study the effects of intramuscular injection of atropine on static and dynamic muscular strength and endurance as well as performance and learning on a gross motor task (GMPT), a multiple dose (o) (saline), 0.5, 1.0 and 2.0 mg), double blind design was utilized. Initially, 7 male volunteers were exposed to 4 days of treadmill walking (3 mph) for 2 hours each day in a hot, dry (40°C, 30% RH) environment to develop a state of partial acclimatization. This was followed by a series of similar exposures on alternate days. Muscle strength, GMPT and rectal temperature measurements were obtained 3-4 h subsequent to the im injection in the same environmental conditions. No significant changes ($p > .05$) were found using a one way repeated measures ANOVA comparing the 9 test days on the following variables: peak torque of the elbow flexors at 30° and 180°·sec⁻¹; average torque at 180°·sec⁻¹; upright pull strength and hand grip endurance. Significant ($p < .05$) changes across test days were found for maximal handgrip strength, average torque of the elbow flexors at 30°·sec⁻¹ and rectal temperature. The slope of the GMPT performance curve over the 9 test days indicated that there was a learning or familiarization effect. The same test given to a control group in a thermoneutral environment showed gradual increases in performance from day 1 to 7, apparently plateauing at day 8. A significant difference was found in the slopes of the performance curves between the control and experimental groups. Motor performance and motor learning were significantly decremented in the hot, dry environment combined with atropine compared to the thermoneutral environment without atropine.

Key words: Atropine, Heat, Exercise, Muscular strength, Muscular endurance,
Learning.

INTRODUCTION

Based on information provided by the Chemical Warfare Review Commission (2) and other sources (7,11) the threat of chemical attack by the Soviet forces is real. Although historically the use of nerve agents has been limited, it is common knowledge that many countries have the capability of using nerve agents as tactical weapons in time of war (11). Recent and past reports by the press, as well as Congressional approval of money for chemical defense indicate that more than just a minimal concern exists about our preparedness for chemical warfare.

NERVE AGENTS

Nerve agents are so called because they have, as their primary actions, mechanisms which compromise cholinergic innervation. They are organophosphate derivatives (most are esters of phosphoric acid) which irreversibly inhibit acetylcholinesterase. Once these compounds get into the human organism the inhibition of acetylcholinesterase (cholinesterase inhibition) results in a buildup of acetylcholine (Ach) at the affected synaptic junctions. Physiological effects of nerve agents include muscular fatigue, involuntary contractions, possible paralysis, diarrhea, increased secretion of mucous glands, increased sweat rate, lacrimation, salivation and urination.

The extreme toxicity of these compounds makes them very attractive as tactical weapons. They are colorless, or light brown in color, liquids which are quite volatile, and they may persist on terrain and foliage for days or weeks (7).

ANTIDOTES

One antidote for organophosphate poisoning is atropine sulfate. Simply stated, atropine will inhibit the action of acetylcholine (Ach) in autonomic effectors innervated by postganglionic cholinergic nerves (24). Although accepted for use as a combat nerve agent antidote, it can have/cause many serious side effects. These include central nervous system effects, e.g., headache, disorientation and dizziness; ophthalmic disturbances including decreased near vision and accommodation, increased irritation and intraocular pressure; cardiovascular and thermoregulatory effects include increased heart rate, skin temperature, rectal temperature and heat storage (24). These effects are magnified if atropine is administered when the nerve agent is not present, i.e., during false alarm situations or during prophylactic administration. It is possible that these effects may interfere with the successful performance of physical tasks.

It is well documented that the administration of atropine will decrease thermoregulatory sweating (4,5). This is accomplished as the muscarinic effects of Ach are blocked and eccrine sweat gland activity is suppressed (15). As sweat evaporation is the primary heat dissipation mechanism in a hot-dry environment, soldiers who are exercising in this environment would certainly be predisposed to heat illness and, possibly, heat stroke following atropine injection.

PURPOSE

The fact that U.S. soldiers are permitted to carry three 2 mg doses of atropine, for self-therapy, makes accidental or prophylactic injection possible. It is important for a commander to know how atropine may influence a soldier's performance without a nerve agent challenge. Several previous studies have attempted to determine the effect of atropine administration on exercise

performance in thermoneutral and hot environments (4,5) but these studies do not lend themselves to military applications.

Therefore, the purpose of this study was to examine the influence of atropine on physical performance in a field-realistic situation: with soldiers dressed in battle dress uniform (BDU's) in a hot, dry environment. The specific exercise performances measured were muscular strength, muscular endurance and performance on a gross motor task.

TABLE 1. Physical Characteristics of the Subjects. (n=7)

<u>VARIABLES</u>	<u>MEAN</u>	<u>SD</u>
AGE (yr)	24	3
HEIGHT (cm)	173.9	12.0
WEIGHT (kg)	75.7	3.1
BODY FAT (%)	15.1	1.8

Table 2. Dosage Schedule Used in the Study

Day 1	Acclimation
Day 2	Acclimation
Day 3	Acclimation
Day 4	Acclimation
Day 5	0 dose (saline)
Day 6	0.5 mg dose
Day 7	off
Day 8	1.0 mg dose
Day 9	off
Day 10	0 dose (saline)
Day 11	off
Day 12	2.0 mg dose
Day 13	off
Day 14	2.0 mg dose
Day 15	off
Day 16	0 dose (saline)

METHODS

SUBJECTS AND DESIGN

Initially, 8 male soldiers volunteered for the study. Informed consent was obtained and a psychological evaluation questionnaire was administered. As a result of this evaluation, 7 subjects were chosen for inclusion in the study. Their physical characteristics are presented in Table 1. Body fat was estimated from 4 skinfolds using the equations of Durnin and Womersley (8).

Subjects were acclimatized to hot, dry conditions in an environmental chamber prior to actual data collection. This process consisted of 4 days of treadmill walking (3 mph) for 2 hours each day at 40°C, 30% relative humidity. This period was also used to familiarize the subjects with test procedures. The acclimation period was followed by a series of similar environmental exposures with atropine or a placebo on alternate days for a total of 14 days. Table 2 illustrates the dosage schedule used in the study. The measurements reported here were taken from day 3 through 16. A multiple dose, double blind design was utilized with a saline injection (0 mg dose) serving as a placebo. The atropine dosages were 0.5, 1.0 and 2.0 mg.

Each test day subjects reported at approximately 0700 hours. Subjects were clothed in the temperate BDU's. Baseline heart rate (HR) and rectal temperatures (T_{re}) were taken while the subjects were seated in a comfortable (20°C, 40% relative humidity) antechamber. Subsequently, an injection of atropine or placebo was given intramuscular (*im*) into the vastus lateralis. A maximum of 10 min elapsed before subjects entered the heated chamber. The exercise treatment included 2 periods of 50 min of exercise (walking at 3 mph on a treadmill) followed by 10 min of rest. Subjects were permitted to drink water

ad lib. Test procedures were terminated for any participant if T_{re} exceeded 39.5°C , HR exceeded $180 \text{ b}\cdot\text{min}^{-1}$, or the medical monitor recommended the subject's removal from the chamber.

At about 1000 hours subjects underwent 1 h of cognitive and psychological testing. From 1100 to 1200 hours subjects underwent the physical performance testing. In these tests subjects rotated randomly through each of 4 stations (15 min each) which included 1) additional treadmill walking (not reported here), 2) tests of isometric strength and endurance, 3) tests of dynamic strength and 4) a gross motor performance task (GMPT). It should be noted that these data were collected 3-4 hours post injection. Since the GMPT had not been used previously, a separate group of subjects was tested in a thermoneutral environment (21°C , 30% relative humidity) for comparative purposes.

APPARATUS AND PROCEDURES

Isometric strength measures included a hand grip and an upright pull test. The hand grip was performed on a device developed in this laboratory (21) and was patterned after one developed by Mundale (19). The grip was shaped to form with the contour of the hand and fingers in a standard grip position. The grip was placed such that it accounted for a 15° ulnar deviation of the functional hand giving a comfortable subject-device coupling. A turnbuckle allowed adjustments for different hand sizes. Force, generated by the subject on the grip was transferred through the turnbuckle to a force transducer. With the subject in a seated position the handgrip device was used to measure 3 maximum voluntary contractions of 3-5 s each with a 30 s rest period between trials. Force output (kg) was recorded on a strip chart recorder.

The upright pull device was also developed in this laboratory and has been previously described (13). It consisted of a force transducer located in an

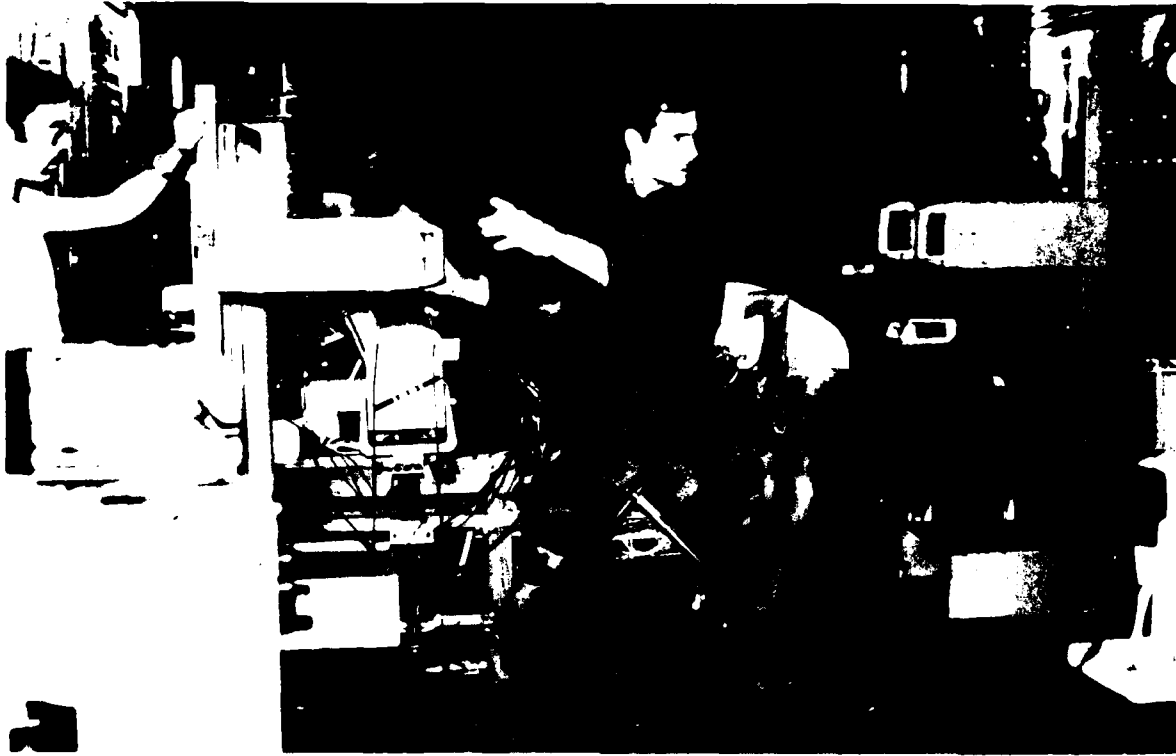


Figure 1. Gross motor performance (GMPT) task device.

aluminum housing and mounted on a plywood platform (79x61cm). The transducer was connected to a chain which was in turn connected by a swivel joint to a handle. The handle was 3.2 cm aluminum tubing 46 cm in length, padded with adhesive tape. The distance from the base platform to the center of the handle was 38 cm. Subjects straddled the transducer with their feet approximately 50 cm apart and assumed a squat position flexing at the knees and hips. The handle was gripped with the palms facing in opposite directions approximately equidistant from the center. Subjects were instructed to place their buttocks against the wall behind them, straighten their backs and look toward the ceiling. A command of "ready, three-two-one-pull" was given and the subject exerted a maximal pull which he held for 3-5 s. Force output (kg) was recorded on a strip chart recorder. The movement involved primarily a combination of hip flexion, knee extension, trunk extension and shoulder elevation.

Hand grip endurance was measured using the same hand grip device as described above. Subjects were asked to exert and hold a force equal to 40% of their maximum voluntary handgrip strength. Subjects monitored their performance on a meter which was adjusted to display their maximal force as 100%. They were instructed to hold the needle on the meter at 40%. The trial was ended when the subject fell 2% below the 40% value for 3 consecutive seconds. The amount of time that the subject held the needle at 40% was recorded in s.

Figure 1 shows the GMPT with a subject standing between the two sets of shelves. During a 1 minute timed interval, the subject removed a 7.3 kg sliding drawer from a shelf at a 150 cm height on the left side, rotated 180° and inserted it into a shelf at a 50 cm height on the right side. Subjects then

repeated this pattern by removing a second sliding drawer from the upper right shelf and inserting this into a shelf on the lower left side. The process was then reversed, moving the shelves from the lower positions back to the higher ones. Subjects repeated these movements as many times as possible in 1 min. The number of repetitions was recorded. A repetition was defined as 1 complete diagonal movement (i.e., upper right to lower left, lower left to upper right, etc.). Four trials (1 min intervals) were performed at each test session with approximately 1 min rest between trials. The mean of the 4 trials comprised the score for the session and this was recorded in repetitions per minute.

For the purposes of the present study, performance on the GMPT was defined as the slope of the regression line when daily performance was plotted against dosage days. This was calculated for 2 conditions, control subjects in a thermoneutral environment (CON-TN) over 8 days and experimental subjects in the heat plus atropine/placebo environment (EXP-HA) over 9 days. Learning was defined as the difference between the initial and final daily performances. For the CON-TN the difference was calculated between days 1 and 8 and for the EXP-HA it was the difference between days 1 and 9.

Isokinetic strength of the elbow flexors (EF) was measured using a Cybex II isokinetic dynamometer. The Cybex chair had a modified seating and arm coupling arrangement as described by Ramos and Knapik (21). Signals from the Cybex were fed to a Grass polygraph strip chart recorder. Subjects performed 3-5 maximal isokinetic contractions at both $30^{\circ}\cdot\text{sec}^{-1}$ and $180^{\circ}\cdot\text{sec}^{-1}$. On each contraction 2 parameters were obtained: peak torque (PT) and average torque (AT). At each velocity the criterion score was the mean of the 3 highest PT values and the corresponding AT values.

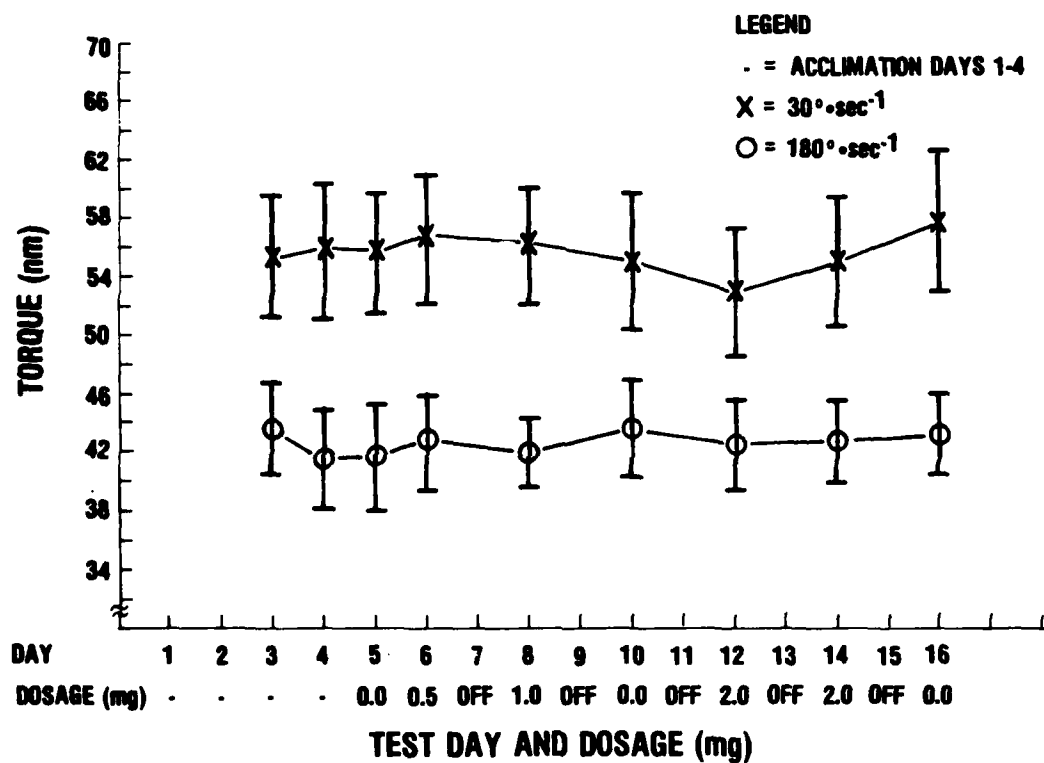


Figure 2. Peak torque of the elbow flexors at two speeds of contraction as a function of days.

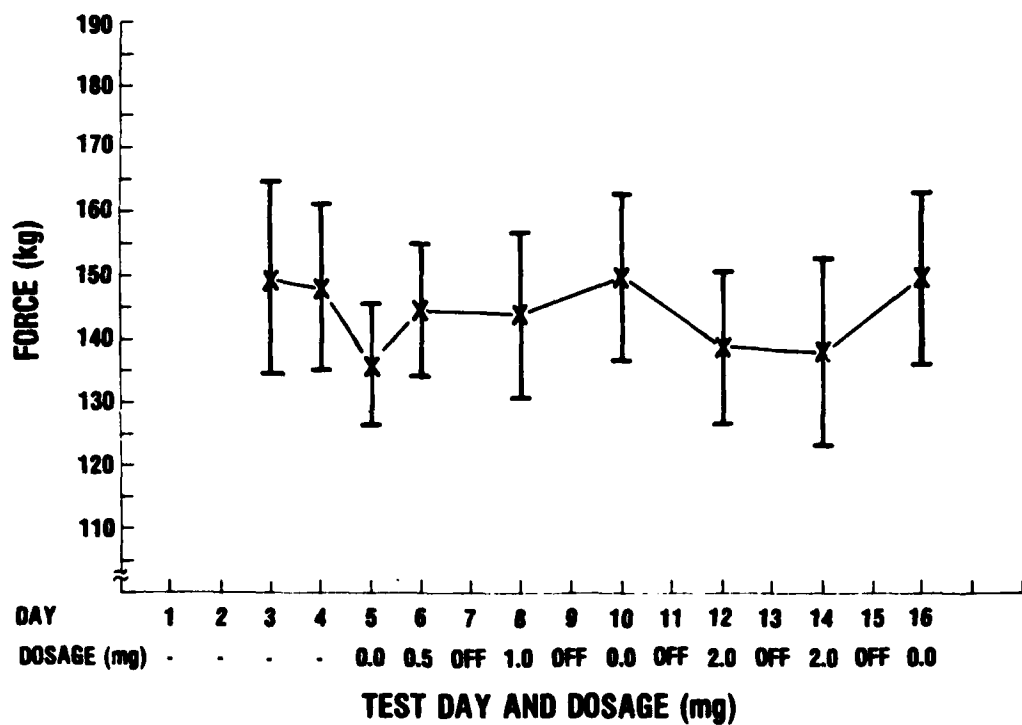


Figure 3a. Mean (\pm SE) upright pull strength plotted as a function of days.

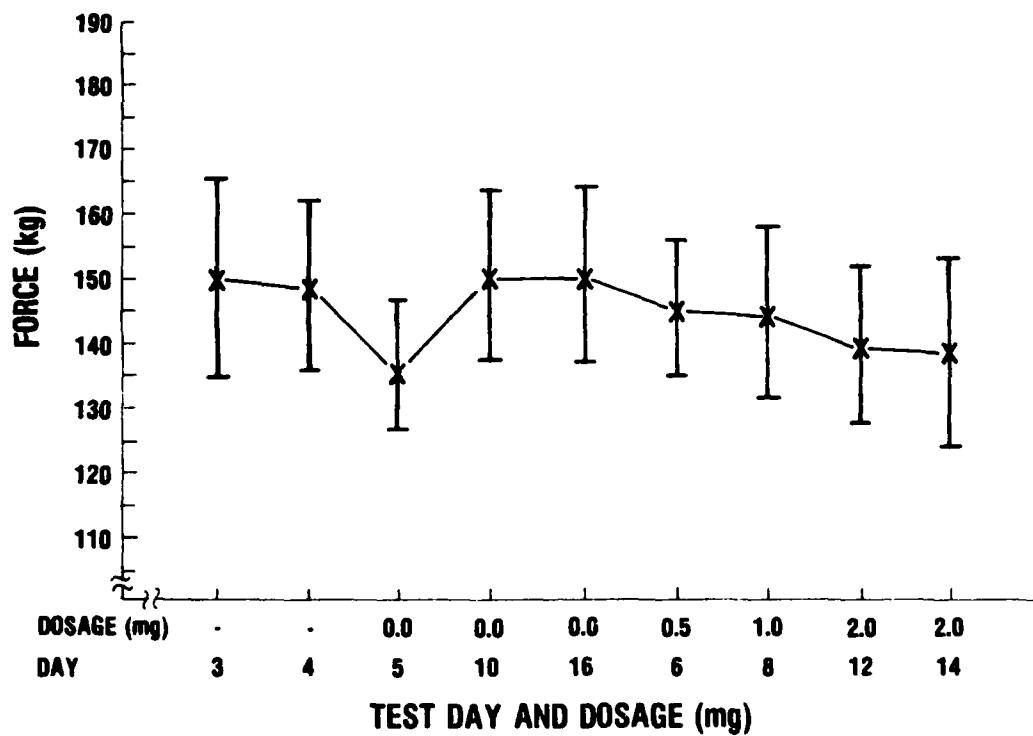


Figure 3b. Mean (\pm SE) upright pull strength plotted as a function of dosage.

PT was the highest torque value obtained during the contraction. In order to obtain AT the instantaneously produced torque was electronically integrated from approximately 40° to 150° of EF. A wheel with 2 elevated spots traveled at the axis of rotation of the lever arm of the Cybex dynamometer and these spots tripped a microswitch at approximately 40° and 150° of EF. When the microswitch was tripped it reset an electronic integrator on the Grass polygraph. The integrator was calibrated with a square wave generator which produced a voltage equivalent to a known amount of AT.

STATISTICAL ANALYSIS

A 1-way analysis of variance (ANOVA) with repeated measures was employed for comparisons of all dosage days for all 7 subjects. A Tukey post hoc analysis was used to interpret significant F statistics. All post hoc analyses are presented in the Appendix. GMPT data were further analyzed using paired and unpaired t-tests. The 0.05 level of statistical significance was set for all analyses.

RESULTS

MUSCLE STRENGTH

Figure 2 shows the isokinetic PT values of the EF at 30° and $180^{\circ}\cdot\text{sec}^{-1}$. A one way repeated measures analysis of variance comparing the 9 test days showed that there were no significant changes at either $30^{\circ}\cdot\text{sec}^{-1}$ ($F(8,47) = 1.10$, $p = 0.38$) or $180^{\circ}\cdot\text{sec}^{-1}$ ($F(8,47) = 0.34$, $p = 0.95$). Similar results were found for upright pull strength as shown in Figures 3a and 3b. There were no significant differences among the 9 test days ($F(8,47) = 1.41$, $p = 0.22$).

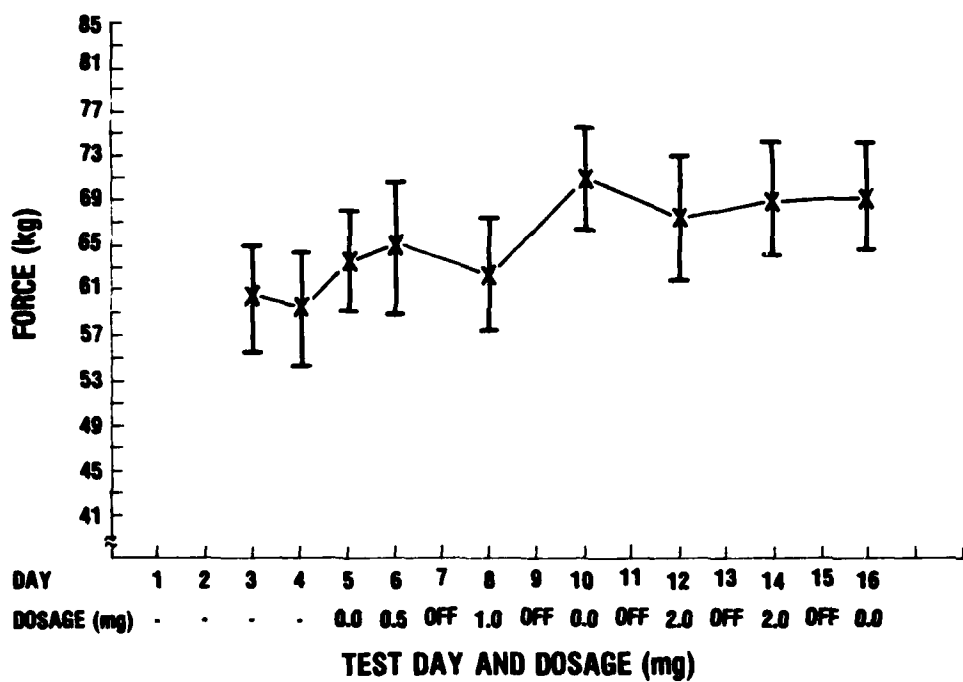


Figure 4a. Mean (\pm SE) hand grip strength plotted as a function of days.

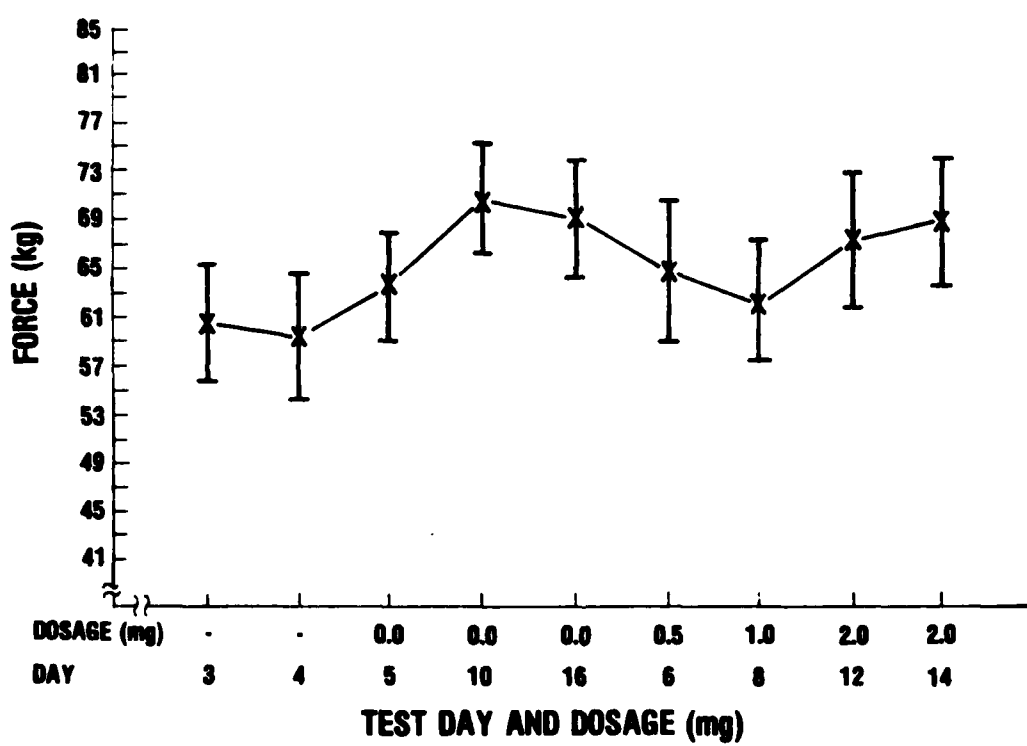


Figure 4b. Mean (\pm SE) hand grip strength plotted as a function of dosage.

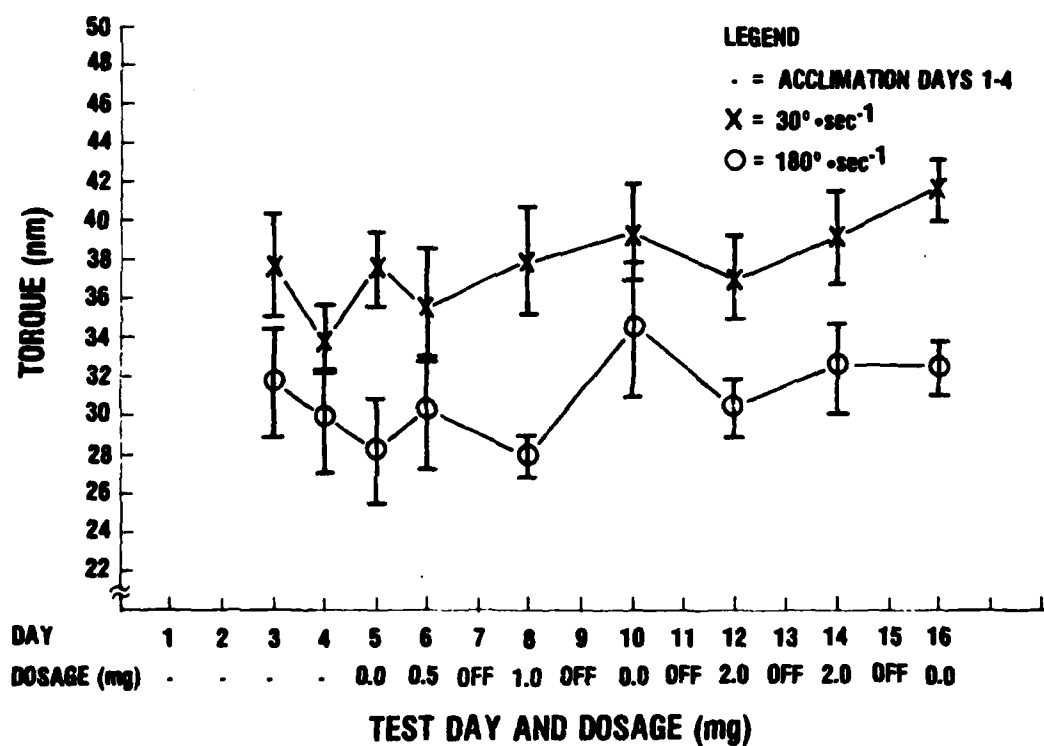


Figure 5a. Mean (\pm SE) isokinetic average torque of the elbow flexors plotted as a function of days.

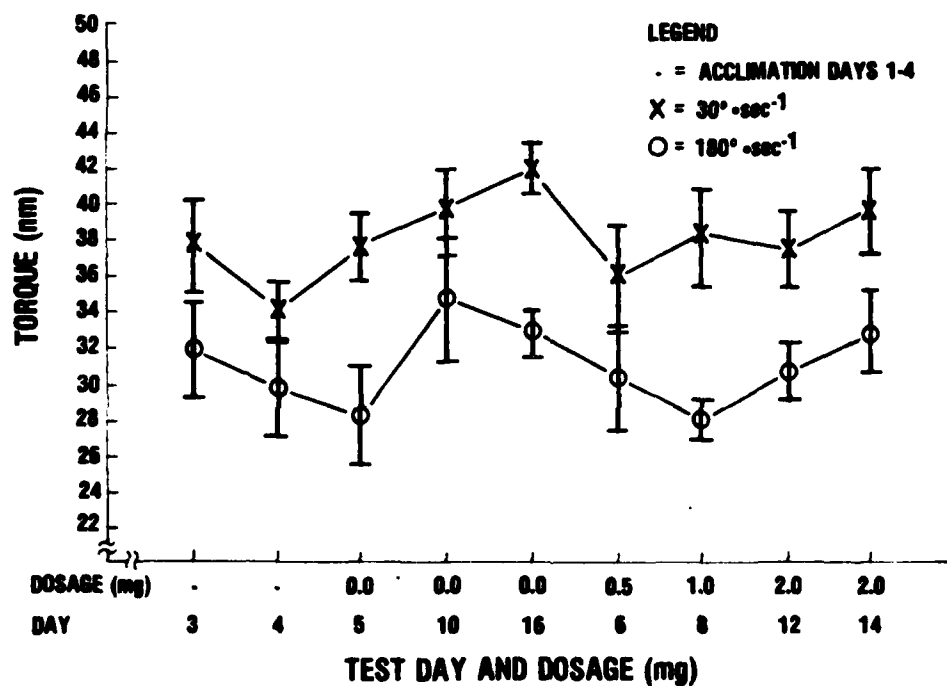


Figure 5b. Mean (\pm SE) isokinetic average torque of the elbow flexors plotted as a function of dosage.

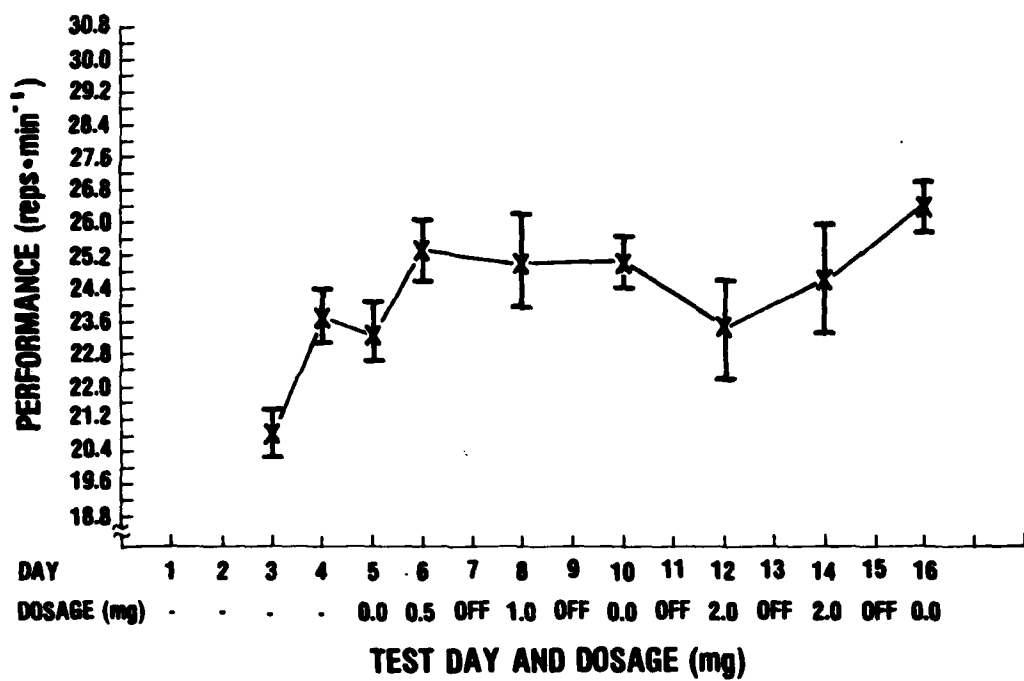


Figure 6a. Performance of experimental subjects during the GMPT as a function of test day.

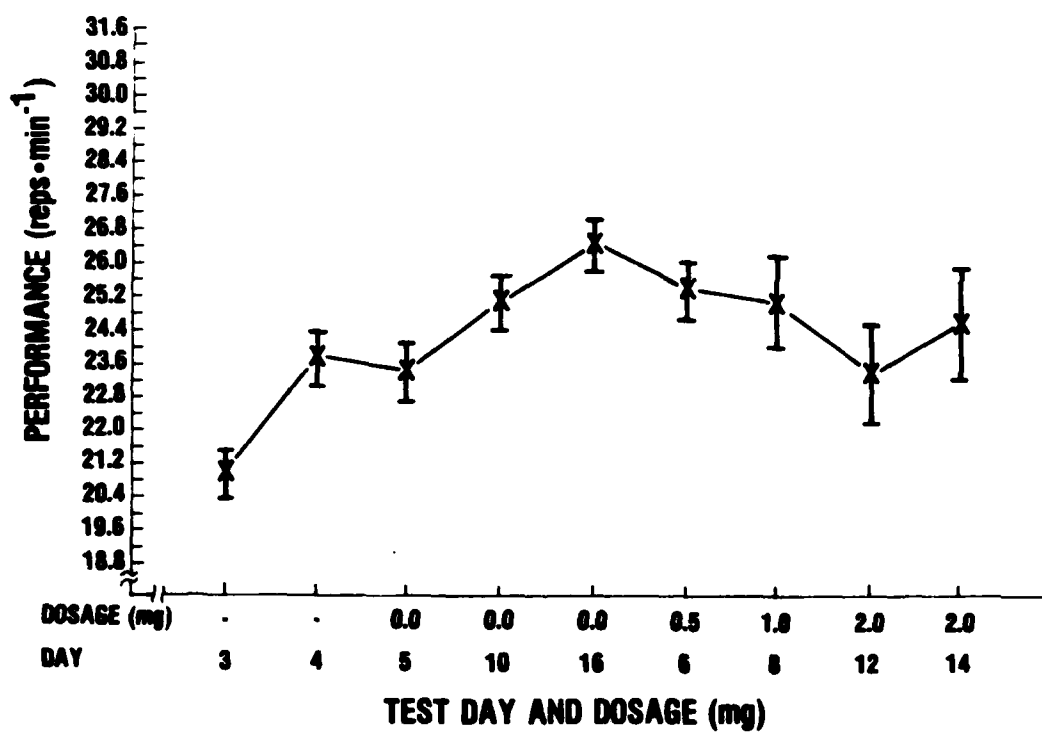


Figure 6b. Performance of the experimental subjects during the GMPT plotted as a function of dosage.

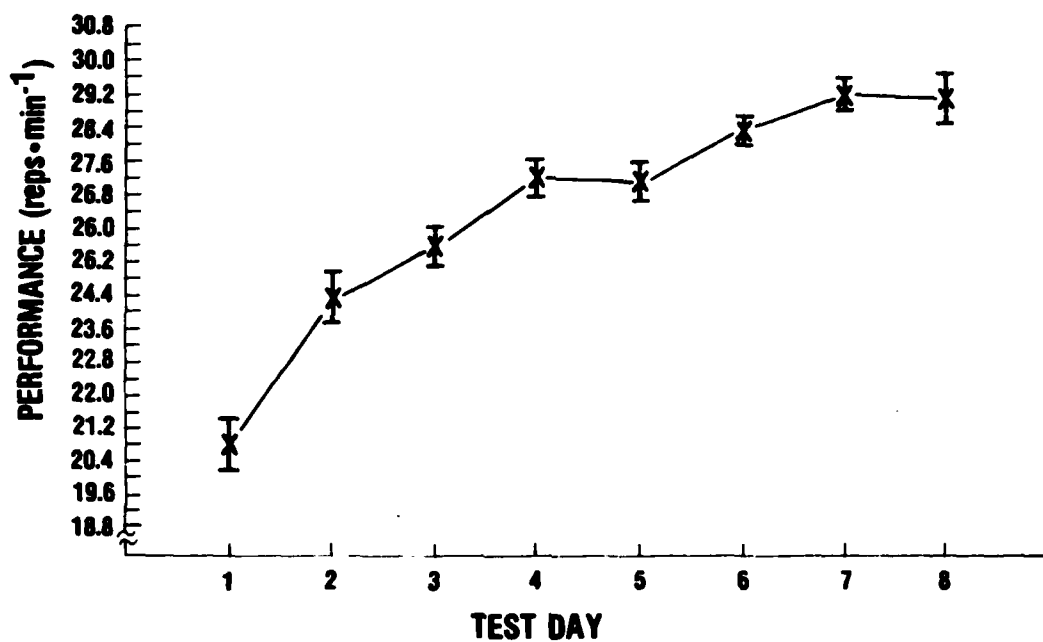


Figure 6c. Performance of the control subjects during the GMPT plotted as a function of test day.

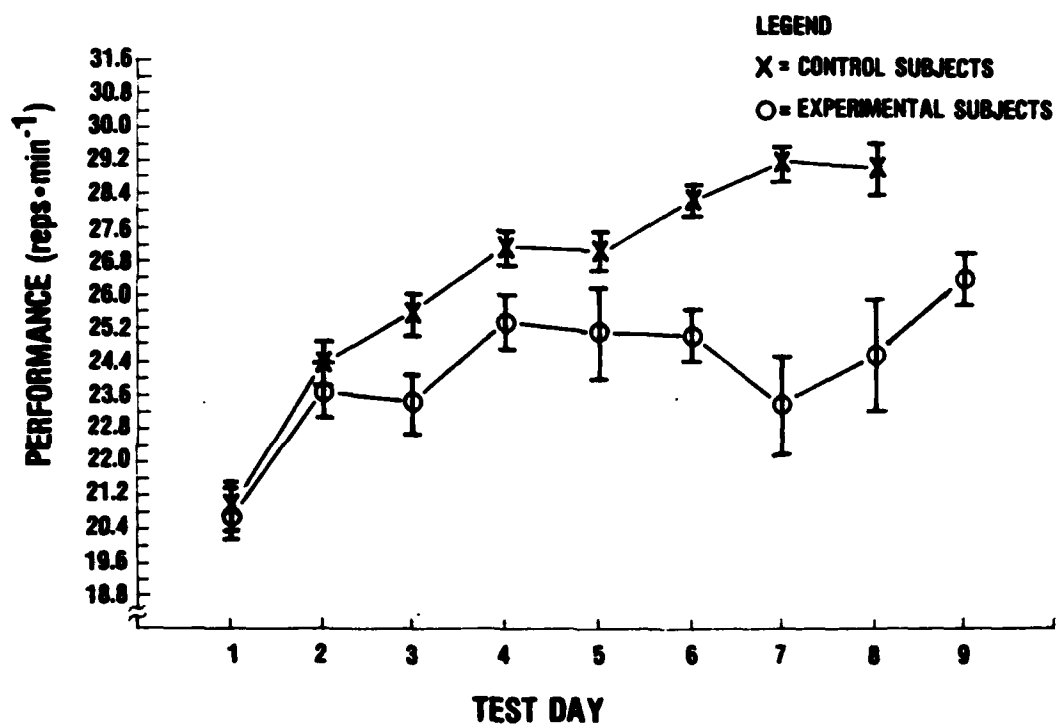


Figure 6d. Performance of the control and experimental subjects plotted as a function of test day.

Table 3. Slopes (reps/day) of the Performance Curves

	N	MEAN	SD	t
CON-TN	5	1.114	0.184	6.65**
EXP-HA	7	0.414	0.209	

CON-TN = Control subjects in a thermoneutral environment

EXP-HA = Experimental subjects in the heat plus atropine environment

** Statistically significant, $p < .01$

Table 4. Learning scores for the GMPT

	N	INITIAL SCORE (reps)	FINAL SCORE (reps)	Δ INITIAL -FINAL (reps)	t-Value
CON-TN	5	20.45	29.10	8.65	15.23**
EXP-HA	7	20.89	24.57	3.68	3.95**

**Statistically significant, $P < .01$

Values of maximal handgrip strength are shown in Figures 4a and 4b. Unlike the other 3 strength measures, there were significant differences across the test days ($F(8,47) = 4.59$ $p < .01$). The Tukey test (appendix) revealed no consistent pattern and ordering the data by dose (Figure 4b) again showed no consistent dose pattern.

Figures 5a and 5b show the values in AT of the EF. At 300-sec^{-1} , the differences among the 9 test days were significant ($F(8,47) = 3.01$, $p < .01$). A dosage affect is not apparent in Figure 5b and the Tukey test (Appendix) revealed no consistent pattern. There was a slight trend for the AT at 300-sec^{-1} to rise over days (Figure 5a). No significant differences were demonstrated in AT at 1800-sec^{-1} ($F(8,47) = 2.10$ $p > .05$).

GROSS MOTOR PERFORMANCE

Figures 6a and 6b show the values of the GMPT. Post hoc visual examination of these data on a day to day basis (see Fig. 6a) suggested that a learning or familiarization effect may have occurred. Characteristics typical of motor learning curves (1,20) were present, especially a curvilinear step-like increase in performance followed by a plateau. To determine if a learning or practice effect was associated with the GMPT, the same test was given to a separate group of 5 healthy males in a thermoneutral environment. The results are presented in Figure 6c. In a thermoneutral environment, performance steadily increased from day 1 to day 7, apparently plateauing at day 8. Figure 6d combines Figures 6a and 6c to show the performance curves in control and experimental conditions. As shown in Table 3 a significant difference was found in the slopes of these 2 lines indicating that performance was significantly higher in the control group. A t-test for independent groups was performed on

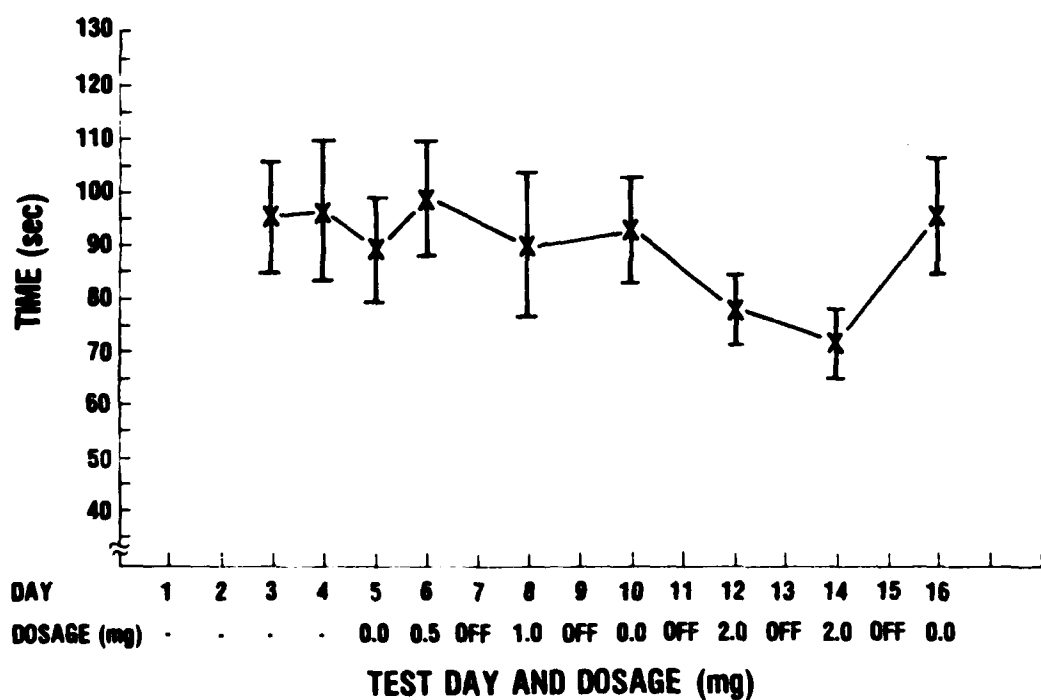


Figure 7a. Mean (\pm SE) hand grip endurance plotted as a function of test day.

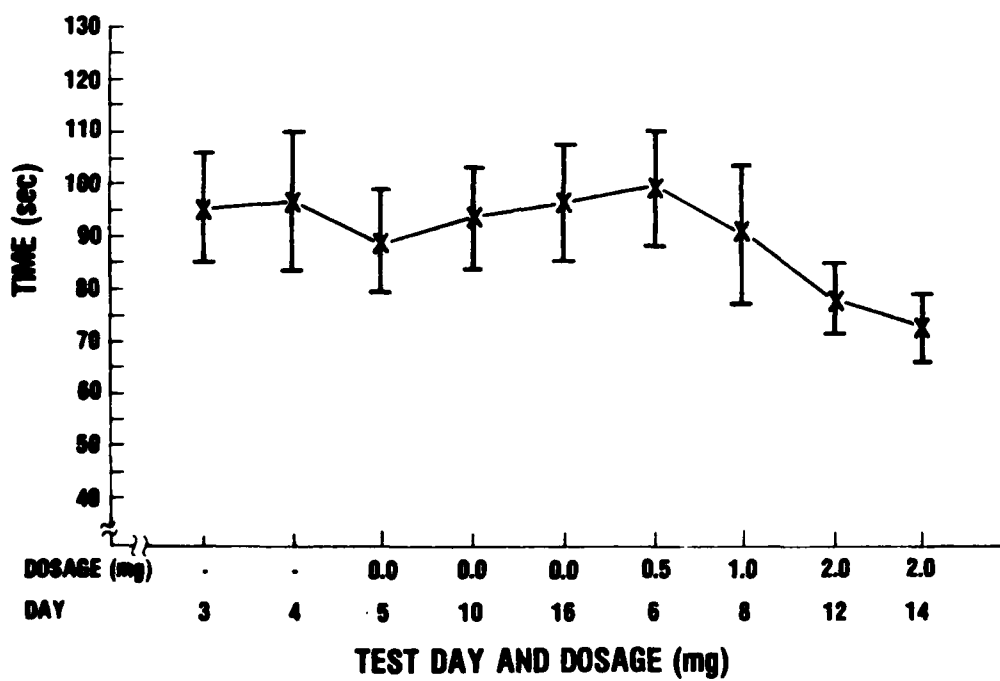


Figure 7b. Mean (\pm SE) hand grip endurance plotted as a function of dosage.

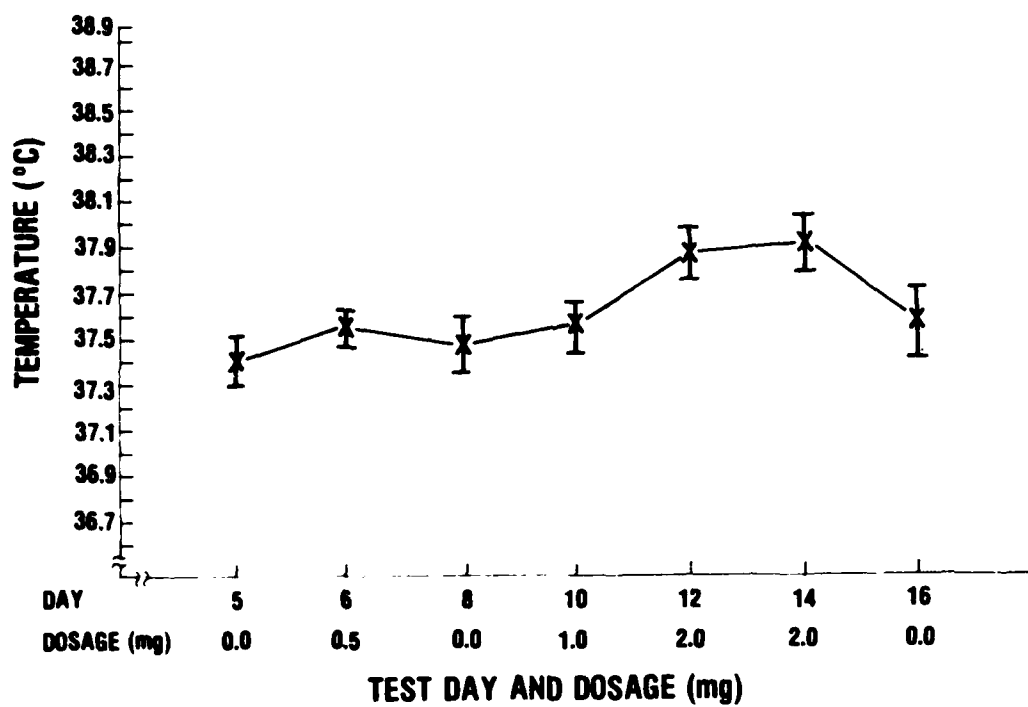


Figure 8a. Mean (\pm SE) rectal temperature plotter as a function of test day.

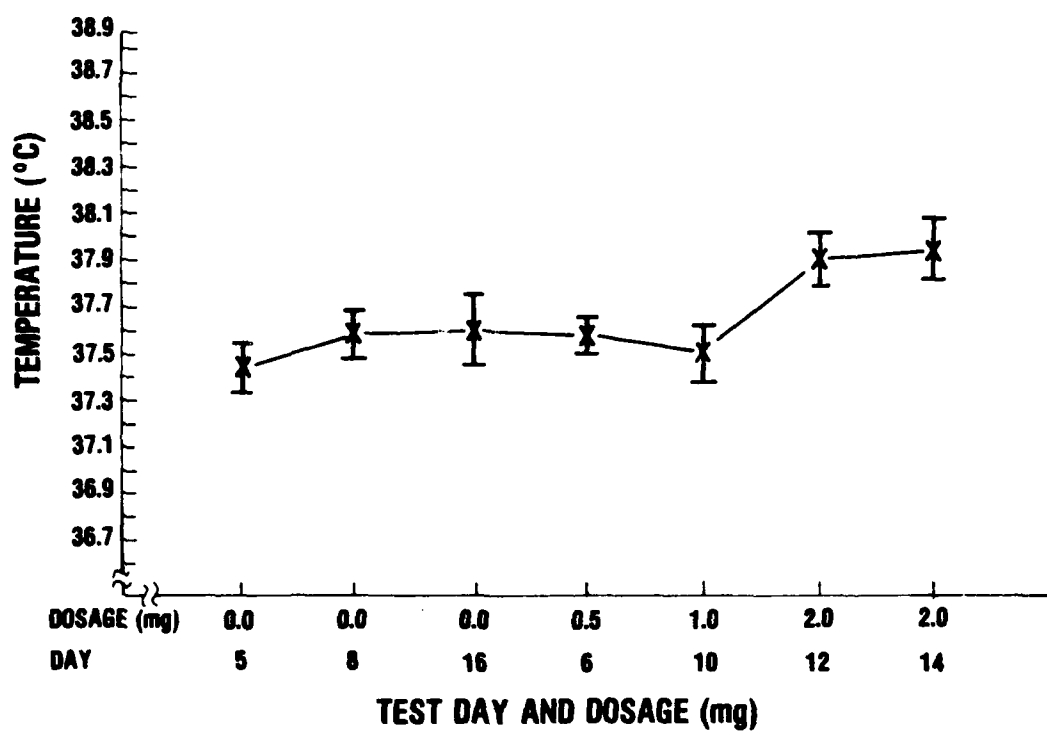


Figure 8b. Mean (\pm SE) rectal temperature plotted as a function of dosage.

trial 1 between both groups. The t-value was not significant ($t = 0.51$, $P > .05$), which indicated that both groups started at the same level of performance.

Table 4 illustrates the comparisons between initial and final scores (learning) for both groups. Significant learning occurred in both test conditions: CON-TN improved by 42% while EXP-HA increased 18%. Learning scores were significantly lower in EXP-HA when compared to CON-TN ($t=4.10$, $p < .01$).

Thus on the GMPT, motor performance and motor learning were significantly decremented in the hot, dry environment combined with atropine compared to a thermoneutral environment without atropine.

HAND GRIP ENDURANCE

Figures 7a and 7b show the changes in hand grip endurance as a function of test days and dosage, respectively. There were no significant differences over days. However, visual examination of Figure 7b suggests that performance on the 2.0 mg days was slightly lower than on the other days.

RECTAL TEMPERATURE

Rectal temperatures across test days and by dosage are presented in Figures 8a and 8b. An ANOVA demonstrated a significant difference across the dosage days ($F(6,39)=5.11$, $p < .01$). The Tukey test (Appendix) indicated that the 2.0 mg dose days had significantly higher temperature than the other days. The average values for the 2.0 mg dose days were 0.38°C higher than the average temperature for the control days.

DISCUSSION

Meyers et al (18) and Headley (11) have summarized the major pharmacologic and performance effects of atropine administration. Atropine injection can potentially cause the most damage to soldiers working in a hot environment because it reduces thermoregulatory sweating by competing for efferent receptor sites in the eccrine sweat gland (15). Several studies have examined the effects of atropine on the thermoregulatory response to exercise in heat (4,5). These studies reported heart rate and rectal temperature increase and sweat rate depression when the dosage was 0.5 to 4.0 mg. However, no data are available to determine if effects carry over to performance involving muscle strength and gross motor performance when measured 3-4 h post injection. Atropine exerts its effects on parasympathetic nerve fibers and therefore should not directly affect muscle strength. However, atropine may indirectly interfere with maximal recruitment of muscle fibers through its central nervous and/or cardiovascular effects (24).

Blood levels of atropine remain elevated up to 6 h after injection (16) and thus it should be possible to detect atropine effects if they are present using the current experimental design. The results of the strength data demonstrate that there was no significant decrement in muscle strength parameters measured 3-4 h after an im administration of atropine in dosages up to 2.0 mg in a hot, dry environment. Neither isokinetic PT of the EF at velocities of either $30^{\circ}\cdot\text{sec}^{-1}$ or $180^{\circ}\cdot\text{sec}^{-1}$ nor isometric strength of the upright pull was affected. While there were some significant changes in HG strength, they occurred with no seemingly consistent pattern. There have been no previous studies on the influence of

atropine on strength in a thermoneutral environment. High external temperatures (up to 48°C) alone do not appear to influence strength (9).

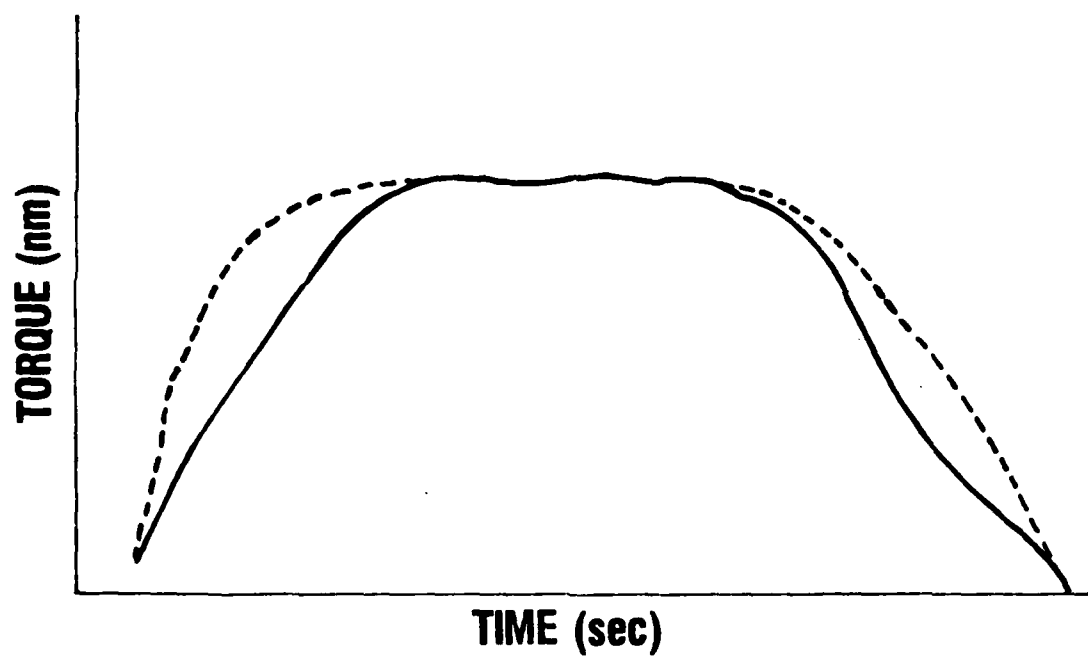


Figure 9. Theoretical curve of the elbow flexors showing a change in average torque without a change in peak torque.

It is of interest that, despite the fact that isokinetic PT of the EF was not influenced by atropine, there were some differences when AT was plotted over days, suggesting a familiarization effect. It has been demonstrated that there are few changes in isokinetic PT at either $30^{\circ}\cdot\text{sec}^{-1}$ or $180^{\circ}\cdot\text{sec}^{-1}$ over days (21), however, there have been no studies that have examined the consistency of AT over days.

It must be remembered that PT and AT were both obtained independently during a single contraction. Any explanation of how AT could change over a series of trials must also account for why there was no change in PT. Figure 9 depicts how this may be possible. As the subject performed the task more often, he became more proficient at the rate at which he developed force and was thus able to produce torque more rapidly early in the contraction. Alternately or concurrently he may also have been able to sustain more force later in the contraction leading to a less rapid decline in torque. Either or both of these changes would increase AT without necessarily influencing PT. It has been shown that the rate of force development (initial rise in the torque or force curve) is not related to either maximal isotonic (3) or isokinetic (22) strength. Further, in a study by Supok and Nelson (23) in which males performed 10 isometric contractions of the EF on each of 10 days, it was found that the rate of tension development increased over days (although in this study there was also an increase in maximal force).

In the present study GMPT showed characteristics of typical learning type tasks (1,20) and thus may be considered a motor learning task. Performance on this test was different in a thermoneutral environment as compared to the hot, dry environment with atropine. Since both the experimental and control groups started at equivalent performance levels it was assumed that these two groups

could be used to discern the effects of an im injection of atropine and heat on learning and performance of this task. Performance and learning were significantly decremented in the atropine plus heat condition.

Overall, the hand grip endurance data indicated no change over the dosage days. However, visual examination of the curve indicates that endurance times were lower on days when 2.0 mg of atropine was administered. Thus, the data suggest that a 2.0 mg dose of atropine may be detrimental to muscular endurance.

Rectal temperatures were significantly elevated during the two 2.0 mg dose days when compared to most of the other dosage days. The 2.0 mg dose of atropine combined with the environmental heat stress was enough to produce a residual effect in T_{re} 3-4 hours post injection. This is important because the soldiers in this study were clothed in the temperate battle dress uniform; it is highly likely that these responses would be exacerbated if the soldier were outfitted in chemical protective clothing.

CONCLUSIONS

A. Intramuscular atropine injection, in dosages of 0.5 to 2.0 mg when measured 3-4 h post injection in a hot, dry environment:

1. Had no significant influence on muscle strength.
2. Did not appear to influence muscular endurance.
3. Caused decrements in performance and learning on the GMPT.

B. Intramuscular atropine injection at a dosage of 2.0 mg resulted in elevated rectal temperature 3-4 h post injection in a hot, dry environment.

C. The GMPT is a rapid motor learning type task. It requires at least 7 days of practice using four 1 min trials with a 1 min rest inter-trial interval per day, before performance will plateau.

D. Future studies involving atropine injection should include measures of muscular endurance and gross motor performance since atropine may influence these aspects of physical performance. While atropine has no significant influence on muscular endurance there was a trend toward lower endurance when the atropine dosage was 2.0 mg.

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Appendix

Tukey Test Results

SUMMARY OF TUKEY TEST COMPUTED ON MAXIMAL HANDGRIP STRENGTH.

HANDGRIP FORCE (kg)	RANK ORDER	DOSE	TEST DAY
59.27	1	0	4
60.17	2	0	3
62.10	3	1.0	8
63.40	4	0	5
64.47	5	0.5	6
67.05	6	2.0	12
68.71	7	2.0	14
68.93	8	0	16
70.56	9	0	10

Mean Square Error: 25.12

Critical Difference: 8.78

Q (47,9): 4.635

NOTE: This post hoc analysis indicated that days 3-8 and 12 were significantly different from days 10,14 and 16. Days 3,5,6,8,12,14 and 16 were different from 4 and 10. Days 5,6,8,12,14 and 16 were different from 3,4 and 10.

SUMMARY OF TUKEY TEST COMPUTED ON AVERAGE TORQUE AT $300\cdot\text{sec}^{-1}$

AVERAGE TORQUE (Nm)	RANK ORDER	DOSE	TEST DAY
33.93	1	0	4
35.67	2	0.5	6
37.14	3	2.0	12
37.46	4	0	5
37.63	5	0	3
37.89	6	1.0	8
39.27	7	2.0	14
39.41	8	0	10
41.66	9	0	16

Mean Square Error: 11.530

Critical Difference: 5.948

Q (47,9): 4.635

NOTE: This post hoc analysis indicated that days 3 through 14 were significantly different from day 16 and that days 3,5,8,10,14 and 16 were significantly different from days 4 and 6.

SUMMARY OF TUKEY TEST RUN ON RECTAL TEMPERATURE DATA.

RECTAL TEMP (°C)	RANK ORDER	DOSE	TEST DAY
37.49	1	0	5
37.55	2	0	8
37.63	3	1.0	10
37.63	4	0.5	6
37.65	5	0	16
37.95	6	2.0	12
38.00	7	2.0	14

Mean Square Error: 0.053

Critical Difference: 0.389

Q (7,34): 4.464

NOTE: This post hoc analysis indicated that days 5,6,8,10 and 16 were significantly different from days 12 and 14. Also, days 6,10,12,14 & 16 were significantly different from days 5 and 8.

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